REC'D 16 MAY 2006
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
P1014PC00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2005/000255	23-02-2005	23-02-2004

International Patent Classification (IPC) or national classification and IPC

See Supplemental Box

Applicant

Sahltech i Göteborg AB et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:

      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report

   ☐ Box No. II Priority

   ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

   ☐ Box No. IV Lack of unity of invention

   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   ☐ Box No. VI Certain documents cited

   ☐ Box No. VII Certain defects in the international application

   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21-09-2005	20-04-2006
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Terese Sandström/Els Telephone No. +46 8 782 25 00

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Cover sheet

International patent classification (IPC)

A61K 48/00 (2006.01)
A61P 19/02 (2006.01)
G01N 33/74 (2006.01)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2005/000255

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

   ☐ international search (Rules 12.3(a) and 23.1(b))

   ☐ publication of the international application (Rule 12.4(a))

   ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

   ☐ the international application as originally filed/furnished

   ☒ the description:

   pages 1-20 as originally filed/furnished

   pages* _____ received by this Authority on _____

   pages* _____ received by this Authority on _____

   ☒ the claims:

   pages _____ as originally filed/furnished

   pages* _____ as amended (together with any statement) under Article 19

   pages* 1 received by this Authority on 03-03-2006

   pages* _____ received by this Authority on _____

   ☒ the drawings:

   pages 1-7 as originally filed/furnished

   pages* _____ received by this Authority on _____

   pages* _____ received by this Authority on _____

   ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages _____

   ☐ the claims, Nos. _____

   ☐ the drawings, sheets/figs _____

   ☐ the sequence listing *(specify)*: _____

   ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages _____

   ☐ the claims, Nos. _____

   ☐ the drawings, sheets/figs _____

   ☐ the sequence listing *(specify)*: _____

   ☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-5	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-5	NO
Industrial applicability (IA)	Claims	1-5	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Documents cited in the International Search Report:

D1: WO03060465 A2
D2: Schäffler A. et al., "Adipocytokines in Synovial Fluid", JAMA, October 2003, Vol. 290, No. 13, pages 1709-1710
D3: WO2004014299 A2

The present claims relate to the use of siRNA molecules targeted to resistin for the manufacture of a medicament for treating rheumatoid arthritis (RA).

D1 discloses the fact that resistin (the document uses the synonym cysteine-rich secreted A12-alpha-like protein 2) is overexpressed in individuals with RA when compared to control individuals not having RA. Methods are disclosed for treating patients with RA by administering antisense molecules targeted to resistin. A number of ways for administration is mentioned, amongst them injection and solutions. (Abstract; page 3, line 26-page 4, line 4; page 6, lines 17-24; page 13, lines 17-21; page 14, lines 6-13; page 44, line 18-page 46, line 11; page 65-page 68, line 6; page 103; page 135; claims.)

D2 shows that resistin is present in synovial fluid of the knee in patient with RA and osteoarthritis (OA). Synovial fluid concentration of resistin was significantly higher in patients with RA than in those with OA. The level of resistin was positively correlated with systemic markers of inflammation such as erythrocyte sedimentation rate and C-reactive protein. Based on the results, the authors suggest the hypothesis that resistin is involved in the inflammatory pathway of RA.

.../...

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of: Box V

Neither D1 nor D2 disclose the use of siRNA molecules targeted to resistin in order to treat RA. Hence, the subject matter claimed in claims 1-5 is novel.

D1 is considered to be one document disclosing the closest prior art.

The subject matter claimed in claim 1 differs from D1 since the present claim 1 uses siRNA molecules and not antisense molecules to decrease the expression/activity of resistin in order to treat RA.

To use siRNA molecules instead of antisense molecules leads to a more simple and effective way of treating RA. A siRNA molecule is not dependent on the secondary structural characteristics of the mRNA molecule to be targeted. A siRNA molecules lead to sequence specific degradation of the target mRNA. Additionally, even very small amounts of siRNA are considered to be effective.

Thus, the problem to be solved is to provide a more simple and effective way of treating RA.

Nowadays, siRNA molecules and their characteristics are well known in this area of research. All the features mention above are known for the person skilled in the art to be features of siRNA molecules. Hence, to use siRNA molecules instead of antisense molecules in order to solve the problem stated above is considered to lie close to hand for a person skilled in the art. Consequently, the subject matter claimed in claim 1 is considered to lack an inventive step in the absence of any demonstrated unexpected or special results.

Additional aspects as claimed in claims 2-5 are either already mentioned in D1 or considered to be detailed executions obvious for a person killed in the art. Thus, also the subject matter claimed in claims 2-5 is considered to lack an inventive step.

D2 is another document considered to disclose the closest prior art.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D2 shows similar results as D1, i.e. a connection between resistin and RA. However, D2 does not suggest any further applications of the results obtained. However, for a person skilled in the art, it seems obvious to draw the conclusion that down-regulation of resistin could be one way of trying to treat RA. Once having drawn that conclusion, the subject matter claimed in claims 1-5 is considered to lie close to hand for the person skilled in the art. This may be argued in a similar manner as for D1 above.

D3 is considered to represent the general state of the art.

To summarise, the subject matter claimed in claims 1-5 is novel but is not considered to involve an inventive step. The subject matter claimed in claims 1-5 is considered to be industrially applicable.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 1 has been amended in an attempt to define the target of the siRNA molecule. However, the wording "a siRNA ***of*** the resistin mRNA" is still a bit unclear. With this present wording, it sounds like the siRNA is a part of the mRNA molecule, which can not be the case since mRNA is single-stranded and a siRNA molecule is double stranded.